REMARKS

Claims 1-14, and 19 are pending in the instant application. Claims 1-14 and 19 have been rejected by the Examiner. By the above amendments, Claims 2, 5, 9, 11 and 14 have been canceled without prejudice and independent Claims 1, 6 and 11 amended to more particularly point out and distinctly claim the subject matter which applicants regard as the invention. More particularly, Claims 1, 6 and 11 have been amended to limit the indication to Alzheimer's dementia and the amount of galantamine as base to 24 mg daily. Applicants submit that the amendments to the claims are supported by the specification as filed, for example, at page 4, lines 36-37, page 6, line 29 and in Claim 5. After entry of the amendments, Claim 1, 3-4, 6-8, 10, 12-13 and 19 will remain pending and under consideration.

The Examiner has maintained the rejection of Claims 1-14 and 19 under 35 U.S.C. §103(a) as being unpatentable over Fulton et al. in view of Yankner et al. (US Patent No. 6,080,778). The Examiner points out that the claims are not limited to Alzheimer's dementia and that the declaration of Dr. Joan Amatniek, submitted with Applicants' prior response dated July 7, 2007, only shows the use of 24 mg of galantamine. The Examiner asserts there is insufficient evidence to establish a synergistic effect with respect to the combination of galantamine and statin since the original trials were not designed to ensure sufficient statistical power to assess the effect of statins, the administration of statins was heterogenous with respect to specific statin, dose and treatment duration and the follow up was limited to 5 to 6 months which may be insufficient for comparing effects of statins and galantamine. The Examiner concludes, "the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been collectively taught by the combined teachings of the references.

Applicants respectfully traverse this rejection. By the above amendments, the claims have been amended to limit the dementia to Alzheimer's dementia and the amount of galantamine (as base) to 24 mg daily. Applicants maintain that the combined teachings of the references (Fulton et al. and Yankner et al.) do not render the amended claims obvious. The Fulton reference, which describes a number of pharmacokinetic and therapeutic studies of galantamine, does not specifically disclose the use of 24 mg per day in any of the studies discussed. Rather, Fulton et

al. describe various human studies wherein: (a) the daily dose of galantamine administered was 5, 10, 15, 30 or 45 mg, or (b) a range of 15-55, 20-50 or 30-50 mg per day of galantamine was administered. Applicants submit that the combined teachings of Fulton et al. and Yankner et al. would not motivate one of ordinary skill in the art to treat Alzheimer's dementia by administering a therapeutically effective amount of galantamine and a statin wherein the amount of galantamine as base is 24 mg daily, as is required by amended Claim 1. Similarly, the combined teachings of the references would not suggest the product or pharmaceutical composition of amended Claims 6 and 10, respectively.

In addition, the claimed invention possesses unexpected advantages which were not suggested by the prior art and which could not have been predicted by one of ordinary skill in the art. As Dr. Amatniek's declaration shows, on the basis of post hoc analyses of several double blind clinical trials of galantamine hydrobromide, Applicants surprisingly found that there was a synergistic positive effect on cognitive function in patients receiving galantamine + statin, as compared to those receiving either galantamine alone or placebo + statin. *See*, Amatniek Decl. ¶¶ 8, 10, 12, 14. Additionally, the data from the initial pivotal trials (GAL-INT1, GAL-USA-1 and GAL-USA-10) unexpectedly and surprisingly showed that patients receiving galantamine + statin were above their baseline scores for 4 more months compared to patients receiving galantamine alone, which is also consistent with a synergistic effect; patients receiving galantamine + statin returned to their original cognitive status at approximately 14 months, as compared to 10 months for the patients on galantamine alone and 3 months for patients on placebo + statin. *See*, Amatniek Decl. ¶¶ 8, 10, 14. Furthermore, at 18 and 24 months, a sustained efficacy difference in favor of galantamine + statin compared to galantamine alone appears to exist, which is also consistent with a synergistic effect. *See*, Amatniek Decl. ¶¶ 8, 10, 14. These unexpected findings rebut any *prima facie* case of obviousness, as one of ordinary skill in the art at the time the invention was made would not have expected the combination of galantamine + statin to have a synergistic effect on cognitive function of AD patients, or to delay by an additional 4 months the time to cross baseline as compared to patients receiving galantamine alone. Moreover, when the data from the post hoc analyses were presented to nine experts in the field of statins, galantamine, and Alzheimer's disease during the first two weeks of June 2007 under terms of confidentiality, the experts were, in fact, surprised by the findings. *See*, Amatniek Decl. ¶¶ 14. Since the claimed invention as a whole would not have been obvious to one of

ordinary skill in the art at the time the invention was made, Applicants respectfully request that the Examiner withdraw the rejection of Claims 1-14 and 19 under 35 U.S.C. §103(a).

In view of the above amendments and remarks, Applicants maintain that the application is in condition for allowance and passage to issue is earnestly requested.

Respectfully submitted,

/Mary A. Appollina/

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Mary A. Appollina
Attorney for Applicants, Reg. No. 34,087

Johnson & Johnson
One Johnson & Johnson Plaza
New Brunswick, NJ 08933-7003
(732) 524-3742
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